

IN THE CLAIMS:

1-21 (cancelled)

22. (currently amended) A method of detecting activity of a G protein-coupled receptor (GPCR), comprising:

- (a) expressing the GPCR in a cell from an exogenous nucleic acid molecule;
- (b) expressing in the cell a mutant cyclic nucleotide-gated CNG channel comprising at least one mutation that makes the channel more sensitive to cAMP than a channel that does not comprise the mutation;
- (c) exposing the cell to at least one membrane potential dye; and
- (d) measuring detectable fluorescence signals from the dye in the cell indicative of activity of the channel, wherein activity of the channel indicates activity of the GPCR.

23. (original) A method according to claim 22, wherein the CNG channel is expressed from an exogenous nucleic acid.

24. (original) A method according to claim 22, wherein the CNG channel is expressed from the genome of the cell.

25. (cancelled)

26. (currently amended) A method according to claim 22, wherein the dye is ~~a fluorescent dye that~~ can be detected by UV-based imaging systems.

27. (cancelled)

28. (previously presented) A method according to 22, wherein the dye is a voltage sensitive dye.

29. (original) A method according to claim 22, wherein measuring comprises determination of CNG channel activity in a single cell.

30. (original) A method according to claim 29, wherein activation is determined by UV-based fluorescence using a microscope.

31. (original) A method according to claim 30, wherein the microscope is coupled to a computer system.

32. (original) A method according to claim 31, wherein the computer system tracks individual cells and performs statistical analysis.

33. (original) A method according to claim 22, wherein measuring is performed with a multiwell microplate reader.

34. (original) A method according to claim 33, wherein the reader is a fluorometric-based reader with a CCD camera.

35. (original) A method according to claim 33, wherein the reader is a fluorometric-based scanning microplate reader.

36. (previously presented) A method according to claim 22, comprising attaching the cell to a solid surface.

37. (original) A method according to claim 36, wherein the solid surface is selected from the group consisting of slides and multiwell plates.

38. (original) A method according to claim 22, wherein the cell is pretreated with a cAMP analogue before measuring.

39. (original) A method according to claim 22, wherein the cell further expresses a promiscuous G protein.

40. (previously presented) A method according to claim 22, comprising determining ion flux.

41. (previously presented) A method according to claim 40, wherein ion flux is determined by a change in spectral characteristic of a dye.

42. (cancelled)

43. (currently amended) A method of identifying a ligand for a G protein coupled receptor, comprising:

(a) contacting a cell with a compound wherein the cell expresses the receptor and at least one cyclic nucleotide-gated (CNG) channel, wherein the receptor is not endogenous to the cell and the CNG channel is a mutant CNG channel that has been engineered to increase the channel sensitivity to cAMP;

(b) exposing the cell to at least one membrane potential dye; and

(c) measuring detectable fluorescence signals from the dye in the cell indicative of activity of the CNG channel, wherein activation of the CNG channel indicates that the compound is a ligand for the receptor.

44. (original) A method according to claim 43, wherein the CNG channel is expressed from an exogenous nucleic acid.

45. (original) A method according to claim 43, wherein the CNG channel is expressed from the genome of the cell.

46. (cancelled)

47. (currently amended) A method according to claim ~~46~~ 43, wherein the dye ~~is a fluorescent dye that~~ can be detected by UV-based imaging systems.

48. (cancelled)

49. (currently amended) A method according to 46 43, wherein the dye is a voltage potential sensitive dye.

50. (previously presented) A method according to claim 43, wherein measuring comprises determination of CNG channel activity in a single cell.

51. (original) A method according to claim 50, wherein activation is determined by UV-based fluorescence using a microscope.

52. (original) A method according to claim 51, wherein the microscope is coupled to a computer system.

53. (original) A method according to claim 51, wherein the computer system tracks individual cells and performs statistical analysis.

54. (original) A method according to claim 43, wherein measuring is performed with a multiwell microplate reader.

55. (original) A method according to claim 54, wherein the reader is a fluorometric-based reader with a CCD camera.

56. (original) A method according to claim 55, wherein the reader is a fluorometric-based scanning microplate reader.

57. (previously presented) A method according to claim 43, comprising attaching the cell to a solid surface.

58. (original) A method according to claim 57, wherein the solid surface is selected from the group consisting of slides and multiwell plates.

59. (original) A method according to claim 43, wherein the cell is pretreated with a cAMP analogue before being contacted with the ligand.

60. (original) A method according to claim 43, wherein the cell further expresses a promiscuous G protein.

61. (previously presented) A method according to claim 43, comprising determining ion flux.

62. (previously presented) A method according to claim 61, wherein ion flux is determined by a change in spectral characteristic of a dye.

63. (cancelled)

64. (currently amended) A method of identifying an agent that modulates an activity mediated by a GPCR comprising:

(a) contacting a cell with the agent and a ligand for the GPCR wherein the cell expresses the GPCR and at least one cyclic nucleotide-gated (CNG) channel and, wherein the CNG channel is a mutant CNG channel that has been engineered to increase the channel sensitivity to cAMP;

(b) exposing the cell to at least one membrane potential dye; and

(c) measuring detectable fluorescence signals from the dye in the cell indicative of activity of the CNG channel.

65. (previously presented) A method according to claim 64, further comprising:

(c) comparing the activity of the CNG channel to the activity of the channel in the absence of the agent, wherein a difference in the activity of the CNG channel indicates the agent modulates the activity.

66. (original) A method according to claim 64, wherein the CNG channel is expressed from an exogenous nucleic acid.

67. (original) A method according to claim 64, wherein the CNG channel is expressed from the genome of the cell.

68. (cancelled)

69. (currently amended) A method according to claim 64, wherein the dye is a fluorescent dye that can be detected by UV-based imaging systems.

70. (cancelled)

71. (previously presented) A method according to 69, wherein the dye is a voltage sensitive dye.

72. (cancelled)

73. (previously presented) A method according to claim 64, wherein channel activity is determined by UV-based fluorescence using a microscope.

74. (original) A method according to claim 73, wherein the microscope is coupled to a computer system.

75. (original) A method according to claim 74, wherein the computer system tracks individual cells and performs statistical analysis.

76. (original) A method according to claim 64, wherein measuring is performed with a multiwell microplate reader.

77. (original) A method according to claim 76, wherein the reader is a fluorometric-based reader with a CCD camera.

78. (original) A method according to claim 76, wherein the reader is a fluorometric-based scanning microplate reader.

79. (previously presented) A method according to claim 64, comprising attaching the cell to a solid surface.

80. (original) A method according to claim 79, wherein the solid surface is selected from the group consisting of slides and multiwell plates.

81. (original) A method according to claim 64, wherein the cell is pretreated with a cAMP analogue before being contacted with the ligand.

82. (original) A method according to claim 64, wherein the cell further expresses a promiscuous G protein.

83-102 (cancelled)